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ELEVENTH ANNUAL MEETING

FAVORABLE OUTCOMES OF PATIENTS WITH ACUTE MYELOID LEUKEMIA AND *DDX41* MUTATION TREATED WITH LOW INTENSITY TREATMENTS WITH VENETOCLAX

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THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
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INTRODUCTION

DDX41 , located on chromosome 5q35.3, is the most frequently mutated gene in myeloid malignancies with germline predisposition. The resulting DDX41 protein is widely expressed and is involved in multiple and diverse cellular functions. The prognostic impact of *DDX41* mutation in AML remains poorly defined. Responses and outcomes with specific treatments, have not been assessed.

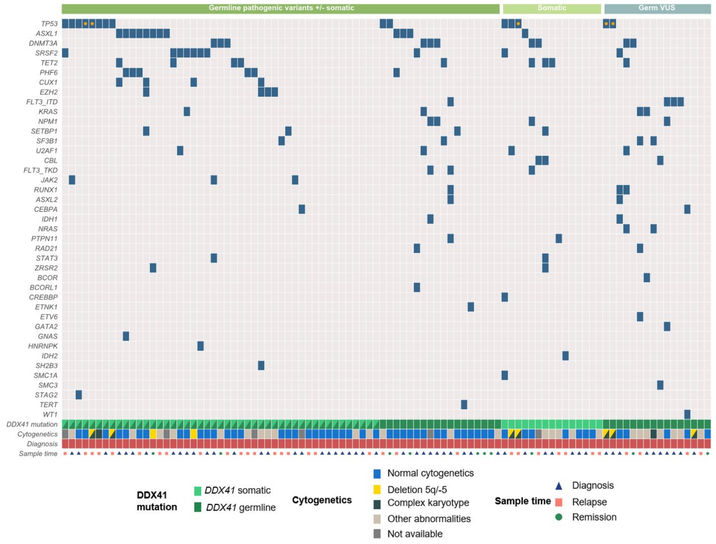
AIM

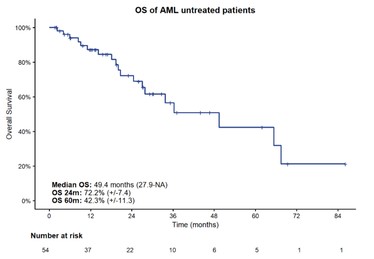
To Analyze a large cohort of patients with AML with *DDX41* mutations, focusing on response to therapies including venetoclax, survival and HSCT outcomes

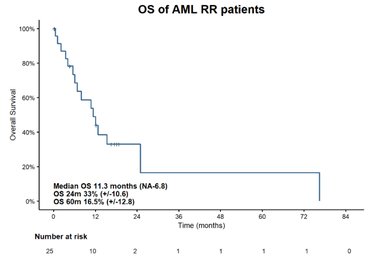
METHODS

- Single-center retrospective study spanning 2010-2022 that included patients with AML with available NGS testing. Among them, patients with *DDX41* mutations were identified and analyzed.
- *DDX41* mutation was performed using targeted NGS testing using an 81-gene panel.
- *DDX41* germline mutation testing was performed using DNA isolated from cultured skin fibroblasts from a skin punch biopsy.
- *DDX41* variants with a VAF <40% were presumed to be somatic variants
- *DDX41* variants with a VAF ≥40% or with confirmation in skin biopsy.
- Germline variants were further classified as pathogenic/likely pathogenic according to the ACMG/AMP guidelines.

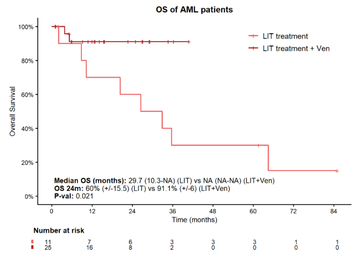
RESULTS & CONCLUSIONS

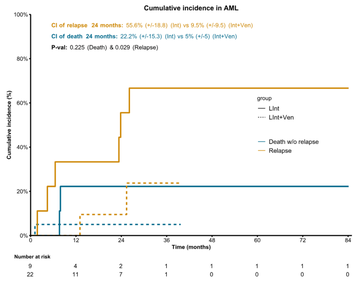






Disease status	Treatment	Response
Previously untreated	Intensive treatment (n=11, 20.4%)	CR: 9 (81.8%)
	Intensive treatment + Venetoclax (n=7, 13%)	CR: 7 (100%)
	Low intensity treatment (n=11, 20.4%)	CR: 8 (63.6%) CRi: 2 (18.2%)
	Low intensity treatment + venetoclax (n=25, 46.2%)	CR: 21 (84%) CRi: 1 (4%)
Relapse/ Refractory	Intensive treatment (n=2, 10.5%)	CR: 1 (50%) CRi: 1 (50%)
	Intensive treatment + Venetoclax (n=1, 10.5%)	CR: 1 (100%)
	Low intensity treatment (n=7, 36.8%)	CR: 2 (28.6%) CRi: 1 (14.3%) PR: 1 (14.3%) MLFS: 1 (14.3%)
	Low intensity treatment + venetoclax (n=4, 21.2%)	CR: 1 (25%) CRi: 1 (25%)
	Other (n=5, 26.3%)	CR: 1 (20%) CRi: 1 (20%)





	AML patients (n=96)
Age, years	69 (21-90)
Sex male, n (%)	72 (75%)
WBC, median (range)	1.95 (0.2-118.7)
ANC, median (range)	0.5 (0-4.3)
Hgb, median (range)	9.3 (5.8-14.5)
Platelets, median (range)	48 (8-591)
BM blasts, median (range)	28 (8-91)
Cytogenetics	**Diploid:** 53 (54.6%) **Abn 5/5q:** 9 (9.3%) **Abn 7:** 10 (10.3%) **+8:** 2 (2.1%) **CBF:** 2 (2.1%) **Complex:** 9 (9.3%)
ELN 2017/ ELN 2022	**Favorable:** 7 (7.3%) / 6 (6.2%) **Intermediate:** 47 (49%) / 30 (31.2%) **Adverse:** 40 (41.7%) / 58 (60.4%) **No classifiable:** 2 (2.1%) / 2 (2.1%)
AML subtype	**AML:** 54 (56.2%) **APL:** 2 (2.1%) **sAML:** 11 (11.5%) **AML R/R:** 29 (30.2%)
DDX41 mutations	**Somatic:** 15 (15%) **Germline:** 18 (19%) **Somatic + Germline:** 47 (49%) **VUS:** 16 (17%)

Conclusions

- Most patients with *DDX41* mutations have a combination of germline and somatic mutation
- Normal karyotype is a common finding in *DDX41* mutated AML
- Patients with AML with *DDX41* mutation treated with LIT with Venetoclax have an improved survival and a lower incidence of disease relapse.

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